**Supplementary Figure Legends**

**Supplementary Figure S1. *In vitro* venetoclax response in representative human patient-derived DLBCL (26) and MCL (10) cell lines.** (A) Immunoblotting of BCL-2 levels in representative MCL and DLBCL cell lines with actin as a loading control. Cell viability assays were performed using the Celltiter-Glo Luminescent Cell Viability Assay in representative GCB-DLBCL (B), non-GCB-DLBCL (C), and MCL (D) cell lines treated with increasing concentrations of venetoclax.

**Supplementary Figure S2. Effects of ibrutinib and idelalisib on MCL cells.** Cell viability assays were performed using the Celltiter-Glo Luminescent Cell Viability Assay in representative MCL primary cells (PT-2 and PT-6) treated with increasing concentrations of ibrutinib (A) or idelalisib (B).

**Supplementary Figure S3.** **Targeting PI3K signaling in combination with venetoclax.** (A) Representative venetoclax-resistant (BJAB and HT) cell lines were treated with venetoclax at a 1:1 ratio drug combinations with PI3K inhibitors (idelalisib and KA2237) or an AKT inhibitor (MK-2206) in a concentration-dependent manner for 72 h, and cell viability was assessed. The highest starting concentration for each drug was 20 mM. The following are the drug combinations: 100 nM: 20 mM; 50 nM:10 mM; 25 nM:5 mM; 12.5 nM:2.5 mM; 6.25 nM:1.25 mM; 3.1 nM:0.61 mM; 1.5 nM:0.3 mM. Data from two independent experiments performed in triplicate are shown. (B) MAPK-pT202-Y204, MEK1-pS217-S221, and JNK-pT183-Y185 protein levels were plotted against the corresponding venetoclax IC50 for each cell line. Spearman’s rank correlation coefficient, and p values determined of the above analysis. P values less than 0.05 indicate significant correlations.

**Supplementary Figure S4.** **RPPA analysis of Mino parental (Mino-P) vs. Mino-venetoclax resistant (Mino-VR) cell lines.** Representative heatmap showing the up and downregulated proteins in the Mino parental (Mino-P) vs. Mino-venetoclax resistant (Mino-VR) cell lines.